Author's response to reviews

Title: A retrospective case-control study of hepatitis C virus infection and oral lichen planus in Japan: association with mutations in the core and NS5A region of hepatitis C virus

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Author's response to reviews: see over
To the Editor

We would like to submit to “Original Article” the enclosed manuscript entitled “A retrospective case-control study of hepatitis C virus infection and oral lichen planus in Japan: association with mutations in the core and NS5A region of hepatitis C virus (Nagao et al)”.

Currently, the number of yearly deaths in Japan due to liver cancers, including hepatocellular carcinoma (HCC), is over 30,000, approximately 80% of which are caused by a persistent hepatitis C virus (HCV). HCV is associated with a broad spectrum of clinical and biological extrahepatic manifestations. Oral lichen planus is common among HCV-infected patients in Japan. The aims of this study were to assess the prevalence of HCV infection in Japanese patients with oral lichen planus and identify the impact of amino acid (aa) substitutions in the HCV core region and IFN-sensitivity–determining region (ISDR) of nonstructural protein 5A (NS5A) associated with lichen planus.

In this retrospective study, 59 patients (group 1-A) with oral lichen planus among 226 consecutive patients who visited our hospital and 116 individuals (group 1-B, controls) with normal oral mucosa were investigated for the presence of liver disease and HCV infection. We compared aa substitutions in the HCV core region (70 and/or 91) and ISDR of NS5A of 12 patients with oral lichen planus (group 2-A) and 7 patients who did not have lichen planus (group 2-B) among patients (high viral loads, genotype 1b) who received interferon (IFN) therapy in group 1-A.

The prevalence of anti-HCV and HCV RNA was 67.80% and 59.32%, respectively, in group 1-A and 25.00% and 13.79%, respectively, in group 1-B. The prevalence of anti-HCV (P<0.0001) and HCV RNA (P<0.0001) in group 1-A was significantly higher than those in group 1-B. According to multivariate analysis, four factors – positivity for HCV RNA, low albumin level (<4.0 g/dL), age 60 years or older, and history of smoking - were associated with the development of oral lichen planus. The adjusted odds ratios for these four factors were 7.68, 3.62, 3.03 and 2.73, respectively, and each was statistically significant. No significant differences in viral factors, such as aa substitutions in the core region and ISDR of NS5A, were detected between the two groups (groups 2-A and -B).

In conclusion, our data show that HCV infection could be the main pathogenic factor of lichen planus in Japanese patients. Routine HCV testing and medical examination for lichen planus are recommended for patients in high-risk HCV areas like Japan.

We believe that we are reporting on an issue of great interest to clinicians.

The author warrants that the article is original, is not under consideration of another journal and has not been previously published. We sign for and accept responsibility for this material on behalf of any and all coauthors.

The attached paper titled "A retrospective case-control study of hepatitis C virus infection and oral lichen planus in Japan: association with mutations in the core and NS5A region of hepatitis C virus" has been carefully reviewed by an experienced medical editor whose first language is English and who is specialized in the editing of papers written by physicians and scientists whose native language is not English.

Thank you for your consideration in advance.

Sincerely yours,

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RE: Revised manuscript of # 3946547576405814

“A retrospective case-control study of hepatitis C virus infection and oral lichen planus in Japan: association with mutations in the core and NS5A region of hepatitis C virus”

To the Editor

Thank you for your novel comments to the manuscript # 3946547576405814. We have answered each criticism point by point in the revised manuscript as follows. I send you my revised manuscript.

Major revisions
Ethical approval:
   Answer: We have changed and added the new sentences in the Methods.

Minor revisions
Methods
Serological assays: We have changed “Serum samples from the 197 subjects…” to “Serum samples from the 175 subjects…”.

We are looking forward to hearing from you at your earliest chance.

Sincerely yours,

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